Prox1 physically and functionally interacts with COUP-TFII to specify lymphatic endothelial cell fate.

Journal: Blood

Publication Year: 2009

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PubMed link: 18815287

Funding Grants: CIRM Stem Cell Biology Training Grant

Public Summary:
We propose that the physical and functional interactions of the 2 proteins constitute an essential part in the program specifying lymphatic endothelial cells (LECs)fate and may provide the molecular basis for the hypothesis of venous endothelial cell (EC)identity being the prerequisite for LEC specification

Scientific Abstract:
Specification of endothelial cell (EC) fate during vascular development is controlled by distinct key regulators. While Notch plays an essential role in induction of arterial phenotypes, COUP-TFII is required to maintain the venous EC identity. Homeodomain transcription factor Prox1 functions to reprogram venous ECs to lymphatic endothelial cells (LECs). Here, we report that the venous EC fate regulator COUP-TFII is expressed in LECs throughout development and physically interacts with Prox1 to form a stable complex in various cell types including LECs. We found that COUP-TFII functions as a coregulator of Prox1 to control several lineage-specific genes including VEGFR-3, FGFR-3, and neuropilin-1 and is required along with Prox1 to maintain LEC phenotype. Together, we propose that the physical and functional interactions of the 2 proteins constitute an essential part in the program specifying LEC fate and may provide the molecular basis for the hypothesis of venous EC identity being the prerequisite for LEC specification.